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WAR DEPARTMENT TECHNICAL BULLETIN

SAND-FLY (PAPPATACI, PHLEBOTOMUS) FEVER

War Department, Washington 25, D. C. • • • 8 August 1944

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1. GENERAL. Sand-fly (*Pappataci*, *Phlebotomus*) fever is a disease of military importance because it occurs in many parts of the world where troops are stationed, and because it can incapacitate large numbers of newcomers to an endemic region for periods of 7 to 14 days, at a time when their services are most needed. It occurs during the hot, dry seasons. It is a nonfatal, self-limited disease characterized in most instances by fever of 2, 3, or 4 days' duration, severe frontal headache, pain in the eyes, which are tended to touch and painful on movement, photophobia, pain in the neck, back, and extremities associated with distinct changes in the leukocytes. The purpose of this bulletin is to supply a summary of the existing knowledge of this disease in order to improve diagnosis, prevent unnecessary confusion with dengue, influenza, and malaria, and lead to the utilization of those prophylactic procedures which may diminish the incidence of the disease.

2. GEOGRAPHIC DISTRIBUTION: *a.* The disease occurs throughout the Mediterranean Basin and the Near and Middle East (including Palestine, Syria, Iran, Iraq, Afghanistan, and Arabia), the eastern part of Africa (including Anglo-Egyptian Sudan, the Somalilands, Madagascar, Kenya, and probably other areas), the coast of Crimea, the Azov and Black Sea littoral, the republics of Central Asia (Kazakh, Tadzhik, Uzbek, and Turkmen), the northwestern portion of India, western Burma, and certain parts of southern China.

b. There are suggestive but unconfirmed reports of its presence elsewhere in India, in French West Africa, southern Japan, northern Argentina, and Colombia.

c. Owing to the lack of precise diagnostic criteria, unrecognized cases of the disease may possibly occur in countries other than those enumerated above.

3. ETIOLOGIC AGENT. The disease is caused by a filtrable virus which is present in the blood for at least 24 hours before and after the onset of fever, but is no longer detectable 40 to 48 hours thereafter. The virus is of small size (probably in the same range of magnitude as that of yellow fever which is one of the smallest known viruses), and while it is readily transmissible to human beings, it has not yet been found infectious for any of a large variety of animals which have been tested.

4. INSECT TRANSMISSION. The disease has been transmitted to human beings by the bites of both naturally and experimentally infected sandflies (*Phlebotomus papatasii*). There is reason to believe that these flies acquire the capacity to transmit the disease approximately 7 days after feeding on an infected individual, and continue to be infectious for the remainder of their brief life span. Although the virus is not regularly transmitted from one generation of flies to another, certain experiments indicate that this may occasionally happen. This at present offers the best explanation of the mechanism by which the virus survives the winter season and persists in endemic countries. *Aedes aegypti* and *Culex pipiens* mosquitoes, human fleas (*Pulex irritans*), and bedbugs have failed to transmit the disease from

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one human being to another. No experimental evidence is as yet available regarding the capacity of other species of Phlebotomus, such as *P. pernicousus*, *P. caucasicus*, etc., to transmit the disease.

5. VECTOR-PHLEBOTOMUS PAPATASII. *a. Phlebotomus papatasii* is a small, light yellow, two-winged, hairy fly whose body is about 2 to 3 mm long and somewhat less than 1 mm thick. The body of the female appears distended and red for some hours after a blood meal, and black for several days thereafter. Only the female bites and as a rule does so during the night and early hours of the morning. In persons who are not sensitive to these insects there is neither pain nor local irritation after the initial stab. The bitten site may or may not be marked by a pinpoint, reddish or hemorrhagic spot. However, about 1 to 2 weeks after the primary exposure to such bites, markedly inflamed papules usually appear at almost all of the sites originally bitten. These papules are 2 to 3 mm in diameter, raised about 0.5 mm, pink or red in color and not infrequently vesicular. These lesions may be much larger, possibly conglomerate. At first they have a typical wheal-like appearance with a pale center. They are sometimes even incapacitating, especially on the feet. The lesions are prominent for 4 to 5 days and then slowly disappear; there is usually moderate to severe itching. Once sensitization is established such papules appear earlier after subsequent bites, and in certain hypersensitive people there is an almost immediate urticarial reaction which may produce marked swelling of the eyelids or lips when these sites are bitten. Hypersensitivity appears to last. The same individuals react strongly year after year for many years. Some people, however, apparently do not develop a sensitization to the bites.

b. Adults of *Phlebotomus papatasii* are most prevalent near the ground level, and only small numbers are encountered in upper stories of buildings. Because of their small size and ability to penetrate small aperatures, ordinary screens or mosquito nets fail to exclude them. Their flight is characteristically in short, jerky hops along the walls and ceiling. The flight range is very short. Sandflies found in human habitations originate, in most instances, from breeding sites within a radius of about 50 yards; however, there may be exceptions to this rule. *Phlebotomus papatasii* breeds in rubble, dugouts, cracks in earth, walls, and embankments, garden soil, and other dark protected spots containing moist organic matter. Unlike mosquitoes the larvae are not aquatic, and are killed by too much moisture. As a consequence, their "season" in different localities is much affected by the prevailing rainfall. Under optimum conditions, 4½ to 6 weeks are required for the eggs to develop into the winged insect. The life of the adult is relatively short in hot weather. In the laboratory it is not more than 2 to 3 weeks.

6. CLINICAL MANIFESTATIONS. *a.* Following an incubation period of 3 to 7 days the onset is usually sudden, with chilly sensations, fever, severe headache, usually frontal; pain in the back of the eyes, pain on movement of the eyes, and photophobia are frequent symptoms. Loss of sensation or taste may occur. Almost always there is malaise accompanied by pain and aching in the limbs, back, and neck.

b. The temperature usually reaches its peak within 24 to 48 hours after onset. The highest temperature may vary from less than 100° F to 105° F. The febrile period in the majority of cases is 2, 3, or 4 days. The temperature occasionally rises again after being normal for a day; relapses occurring within a week, or sometimes after longer periods, are occasionally seen. Giddiness, weakness, and feelings of depression are often encountered during convalescence, the duration of which varies with the individual and the climate. No fatalities are recorded among the tens of thousands of cases.

c. The pulse rate may be elevated in proportion to the degree of fever on the first day. Thereafter, it returns to normal more rapidly than does the temperature, and a bradycardia is often present at the end of the febrile period and during convalescence.

d. Other physical findings are limited to an erythema of the face and exposed parts of the neck and chest, conjunctival injection, tenderness of the eyeballs, and some congestion (but not real inflammation) of the fauces, soft palate, and posterior pharyngeal wall. Lymphadenopathy is rare or absent. Enlargement of the liver or spleen is not part of this disease. Eruptions of the urticarial or erythema multi-

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forme types may very occasionally be encountered, but a true rash as seen in dengue does not occur.

7. CLINICAL LABORATORY DATA. *a.* The changes in the leukocytes constitute the only positive clinical laboratory finding in sand-fly fever, and should be utilized whenever possible to aid in the diagnosis. A true leukopenia, that is, a reduction in total count to below 5,000 white cells per cubic millimeter, may be observed in about 90 per cent of the cases when daily counts are done during the febrile period and convalescence. It is important to realize, however, that the leukopenia may not appear until the last day of fever or even several days after defervescence.

b. The Schilling differential is an essential part of the study of the leukocytes since it reveals the most important change which occurs in these cells regardless of whether or not a true leukopenia develops, that is, a marked transitory diminution in the number of segmented neutrophiles, accompanied by a marked increase in the number of immature neutrophiles, chiefly the stab cells. The characteristic finding on the *first day* of the fever is a total count within normal limits, a relative and absolute *decrease* in the lymphocytes, accompanied by a relative and sometimes absolute increase in neutrophiles which is due to an increase in the nonfilament cells. The total number of segmented (filament) cells is usually not decreased at this time. During the *second or third day* of the fever, the number of lymphocytes begins to return to normal and for a few days thereafter may constitute 40 to 65 percent of the total; at the same time the number of segmented neutrophiles begins to drop, and the immature (nonfilament) cells increase to a point at which they usually outnumber the segmented cells. The normal picture usually returns 5 to 8 days after defervescence. At the beginning of an outbreak it is advisable to do leukocyte studies on a number of patients at least every other day, or when that is not possible, at least on three occasions: first, on admission; second, when the temperature has returned to normal; and third, just before discharge or 5 to 8 days after defervescence. Pharyngitis with fever and so-called "grippe" do not show these changes in the leukocytes.

c. The erythrocytes show no changes from normal. The urine is usually normal, although it may be dark and may contain albumin as in any febrile patient.

8. DIFFERENTIAL DIAGNOSIS. *a.* In the absence of a specific test for the individual case, the diagnosis of sand-fly fever must be made on clinical and epidemiological grounds. The occurrence of a clinical syndrome together with changes in the leukocytes of the type described in the preceding paragraphs, during the summer or autumn months in a country known to harbor Phlebotomus flies, may reasonably warrant the diagnosis of sand-fly fever. Dengue, which is perhaps more closely related to sand-fly fever than any other disease, has to be considered in the differential diagnosis of an epidemic in those localities in which both fevers may occur. The following points may aid in the differential diagnosis of these two diseases in a group of patients:

(1) While the duration of fever in both diseases may vary from 1 to 9 days, in dengue approximately 80 percent of the cases exhibit 5-, 6-, or 7-day fevers, while in sand-fly fever more than 80 percent are made up of 2-, 3-, and 4-day fevers.

(2) Lymphadenopathy is common in dengue, uncommon or absent in sand-fly fever.

(3) While a certain proportion of dengue cases may not exhibit it, a rash is nevertheless common in dengue and exceptional in sand-fly fever.

b. Influenza epidemics rarely occur during the hot summer or autumn months, and the signs of inflammation of the respiratory tract which usually accompany this disease, are absent in sand-fly fever. In individual cases, differentiation from pharyngitis with fever, so-called "grippe," or gastroenteritis may be aided by suitable leukocyte studies. In localities where malaria and sand-fly fever occur simultaneously, and when, because of the pressure of events, antimalarial therapy is adminstered in the absence of a positive smear, cases of sand-fly fever may be erroneously diagnosed as malaria.

9. IMMUNITY. There is good reason to believe that the native populations of endemic regions are attacked by the disease in infancy or childhood, and that the immunity of the adolescent and adult populations is the result of previous infection. In view of the fact that

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multiple attacks are not infrequently reported during the same season or in subsequent seasons, some observers doubt that a single attack of the disease produces appreciable immunity. It has been a common military experience, however, that troops which have sustained epidemics of sandfly fever and which remain in endemic areas are immune during subsequent seasons at a time when fresh troops, newly arrived in the area, are being infected.

10. PROPHYLAXIS. Although much remains to be learned about the habits of *Phlebotomus papatasii*, certain steps based on what is now known may be taken to prevent outbreaks of the disease or to modify their course once they have developed.

a. Sleeping quarters should be located on open, elevated, dry, sandy ground when feasible, and as far from native dwellings and domestic animals as possible. The more breeze in a given location, the better.

b. Whenever possible, the area within a radius of 50 to 100 yards of sleeping quarters should be cleared of rubble, detritus, gardens, vegetation, and needless earthen walls or banks. The ground surfaces should be leveled and rendered as impermeable as practicable by filling cracks in the earth, and by tarring or cementing, especially in permanent installations. When such measures are impractical, the ground may be rendered unsuitable for breeding by applying waste motor oil, or creosote; walls and embankments should receive the same treatment.

c. Inside sleeping quarters the following measures should be taken:

(1) Spray at least twice daily with insecticides.
(2) Treat walls with DDT residual spray.
(3) Eliminate cracks and crevices in the walls.
(4) Reduce fixtures to a minimum.
(5) Keep beds, kits, and clothing away from walls where sand flies may seek protection during the daytime.
(6) Utilize electric fans to best advantage whenever available.

d. Sleeping nets of mesh fine enough (more than 45 per inch) to keep out sand flies should be used in heavily infested areas. Application of insect repellent to nets of ordinary mesh may be useful in excluding sand flies.

e. Repellents. After sundown, quartermaster-issue insect repellent should be used on exposed parts of the body. Protection against bites of sand flies lasts for 4 to 6 hours. One application should be made at sundown and a second upon retiring. Regular use of repellent has proved an effective means of preventing sand-fly fever.

f. Protective clothing. Long sleeves and long trousers should be worn, especially after sundown.

11. MANAGEMENT OF PATIENTS. The disease is self-limited, and no specific therapy is available. Symptomatic care, including rest in bed during the febrile period and for at least 24 hours thereafter, ample fluids, and aspirin with or without codeine may be advised. Men should be warned against scratching or irritating the skin lesions caused by sand-fly bites. In order to diminish the chances of spreading infection, patients should be hospitalized, and exposed parts of the body should be treated with insect repellent during the first 2 days of illness. Sleeping nets of mesh fine enough (more than 45 per inch) should also be used, if they can be tolerated. Since hospital epidemics of this disease have been recorded, separate wards for patients with sand-fly fever located at 100 to 200 yards away from other buildings should be established when possible. The period of hospitalization varies with the individual patient. Convalescence may be expected to require about a week.

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